
# Armed Forces College of Medicine

## AFCM

# Calcium Homeostasis

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# INTENDED LEARNING OBJECTIVES (ILO)

- **By the end of this lecture the student will be able to:**

- Mention the normal total and ionized calcium levels.
- List its physiological significances.
- List the hormones involved in its regulation.
- List the functions of calcitonin, describe its regulation.
- Compare between the effects and mechanism of actions of each one.
- Summarize the mechanism of calcium homeostasis.

# Distribution of calcium in the human body

## 1100 gm (approximately 1 Kg)
## (1.5% total body weight)

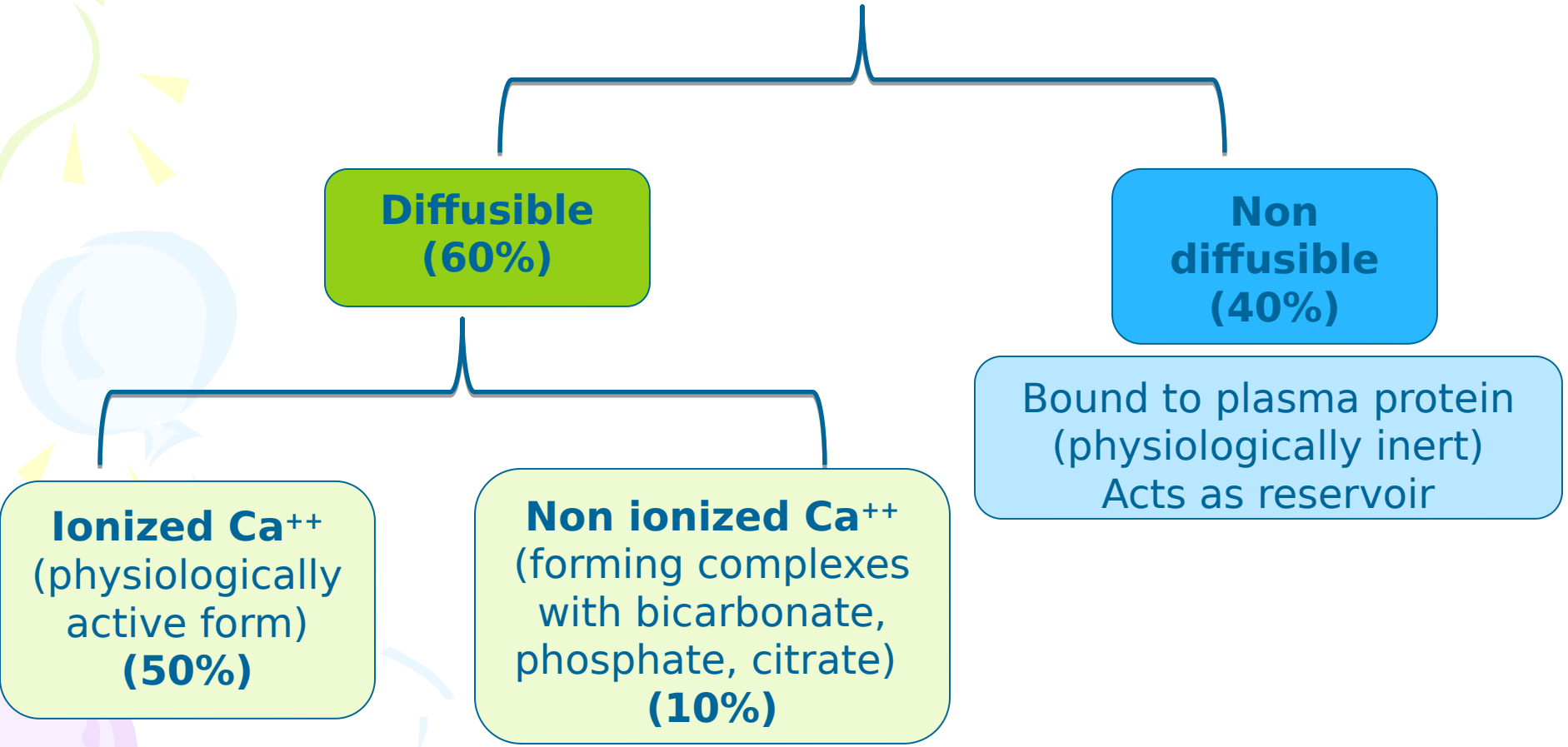
**99 %**
**in the skeleton (bone) ($Ca^{++}$ bank)**

**0.9 %**
**in the ICF (cells) (soft tissue)**

**0.1 %**
**in the ECF (plasma)**

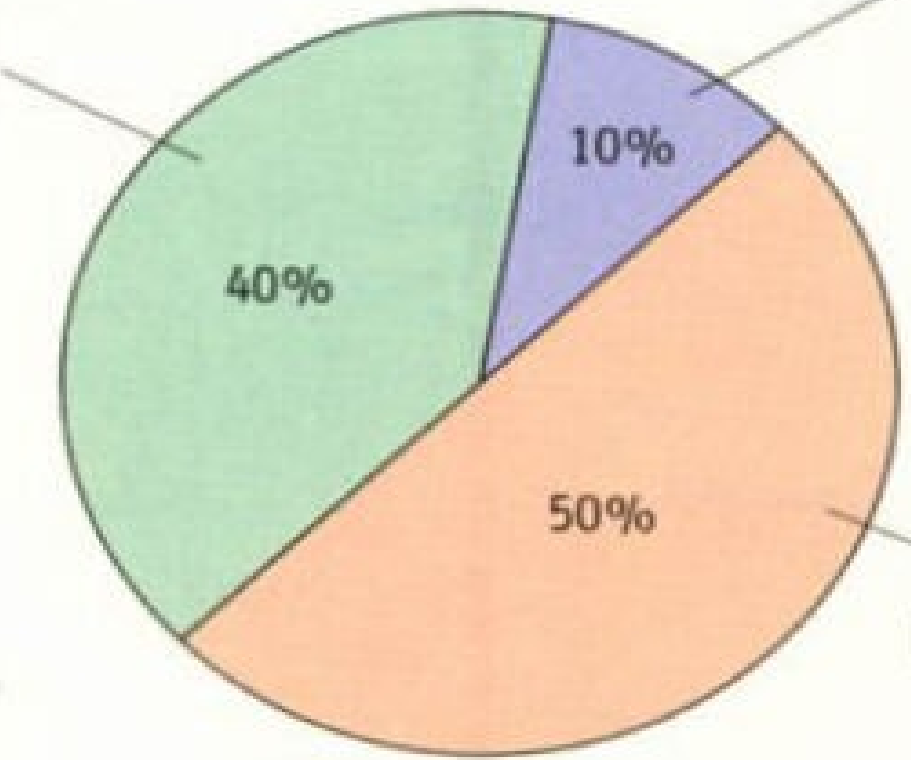
Bones serve as large **$Ca^{++}$ reservoirs**, releasing calcium when its ECF concentration decreases.

# Plasma $Ca^{++}$ level: 9-11 mg/dl (average: 10 mg/dl)



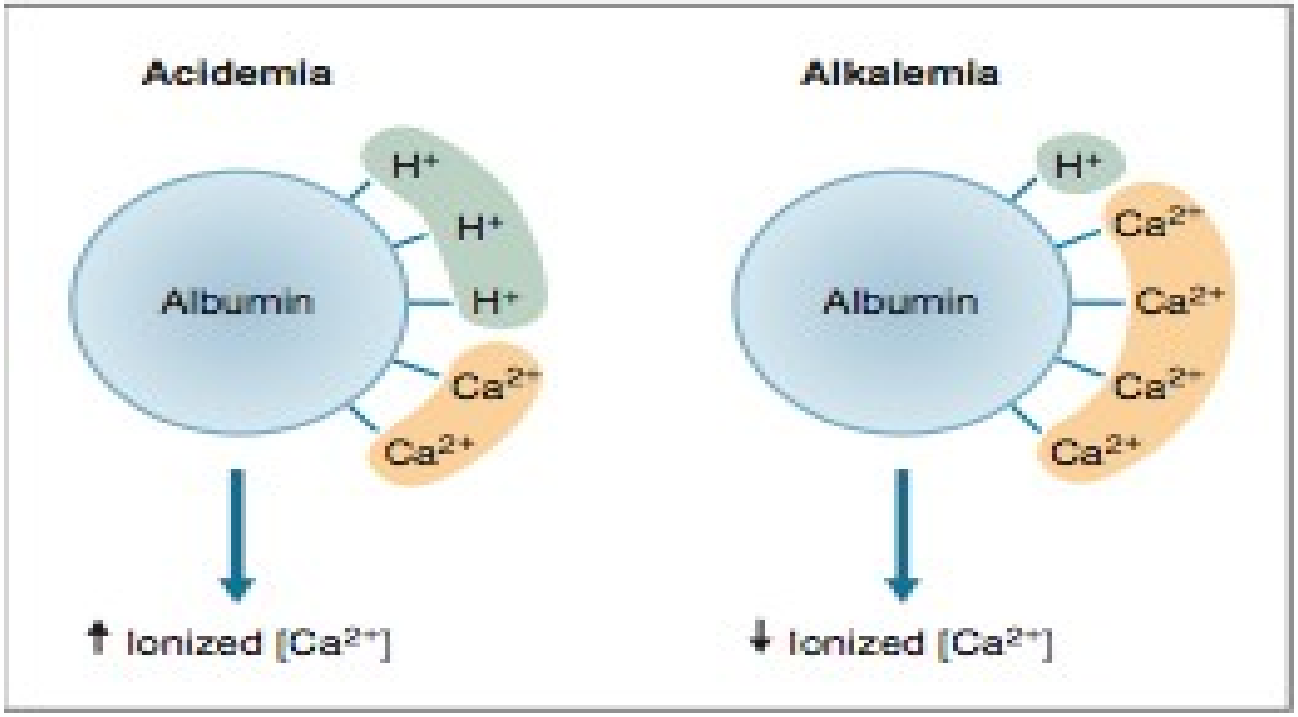

## Three Forms of Circulating $Ca^{2+}$

## Circulating calcium fractions




| total $Ca^{2+}$ | = | ionized $Ca^{2+}$ | + | protein bound $Ca^{2+}$ | + | complexed $Ca^{2+}$ |
|---|---|---|---|---|---|---|
| (2.2–2.6 mmol/L) | | (1.1–1.3 mmol/L) | | (0.9–1.0 mmol/L) | | (0.2–0.3 mmol/L) |

- **Ionized fraction depends on pH:**
  **$Ca^{++}$ protein binding decreases as pH decreases**
  **$Ca^{++}$ protein binding increases as pH increases**




**Alkalosis:** increased calcium binding to protein; **decreased ionized fraction**

pH 7. 45

pH 7.35

**Acidosis:** decreased calcium binding to protein; **increased ionized fraction**

# Distribution of calcium in the human body

Total body $Ca^{2+}$
100%

**Hydroxyapatite**
99%

**0.9% present in the cells (ICF)**

**0.1% present in the ECF:**

Ionized Calcium:
$Ca^{++}$
50%

- *Present as free, active cation*
- *Diffuses easily across capillary membranes*

Protein-bound Calcium:
40%

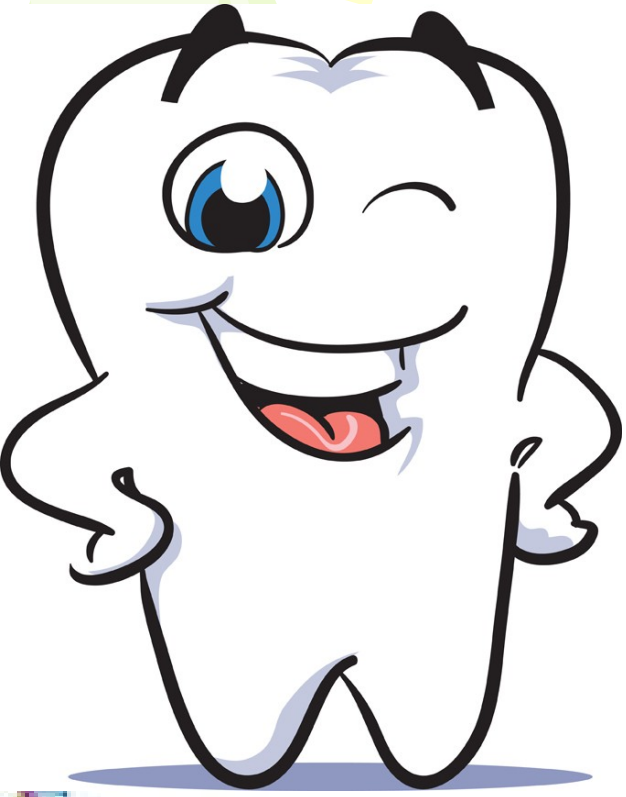
- *Bound mainly to **albumin***
- *Cannot diffuse across capillary membranes*

Anion-bound calcium:
10 %

- *Bound to small anionic molecules, eg. Phosphate, carbonate and citrate*
- *diffuses easily across capillary membranes*

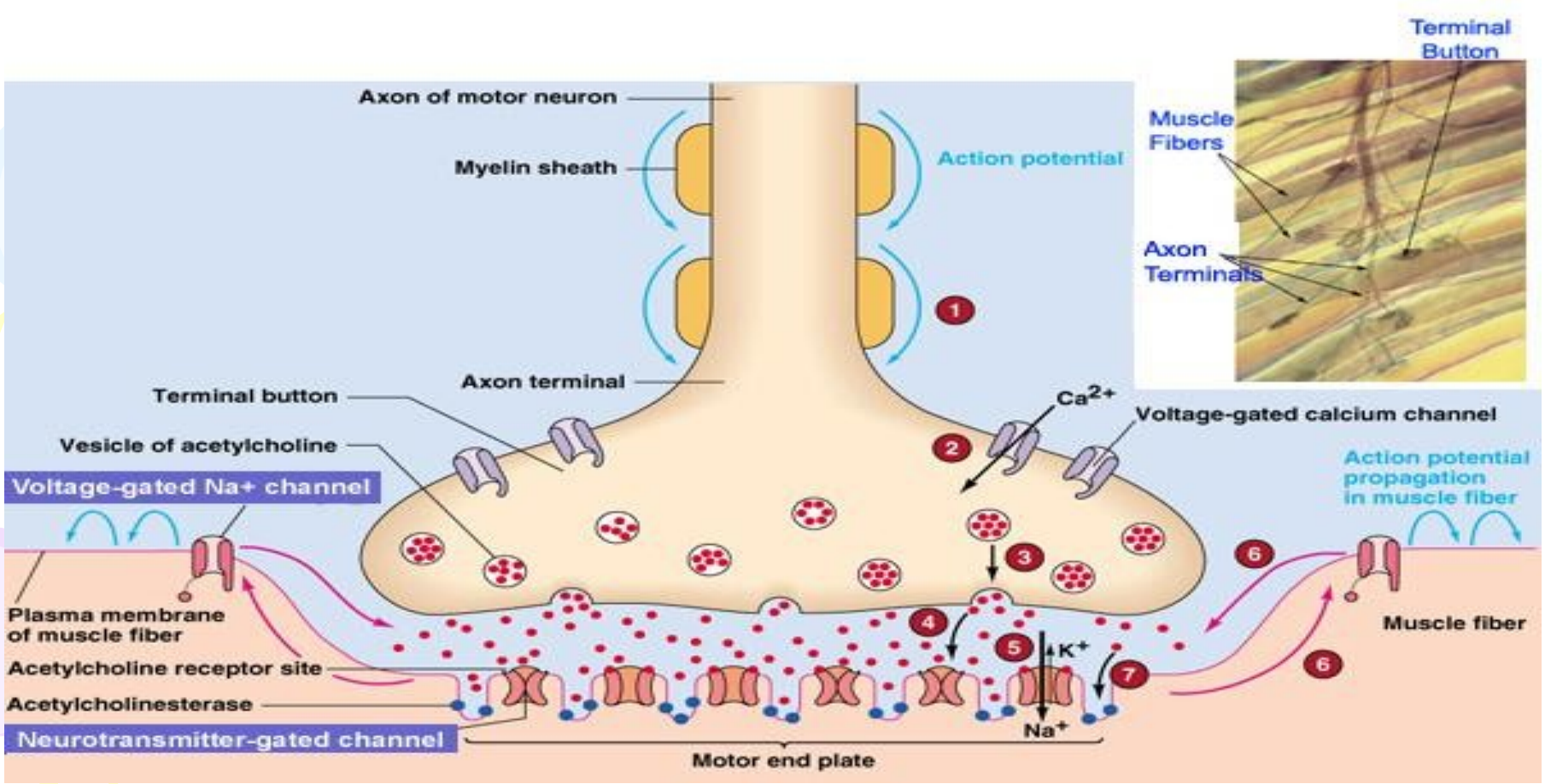
# Functions of Ionic Calcium

## Bone and teeth formation



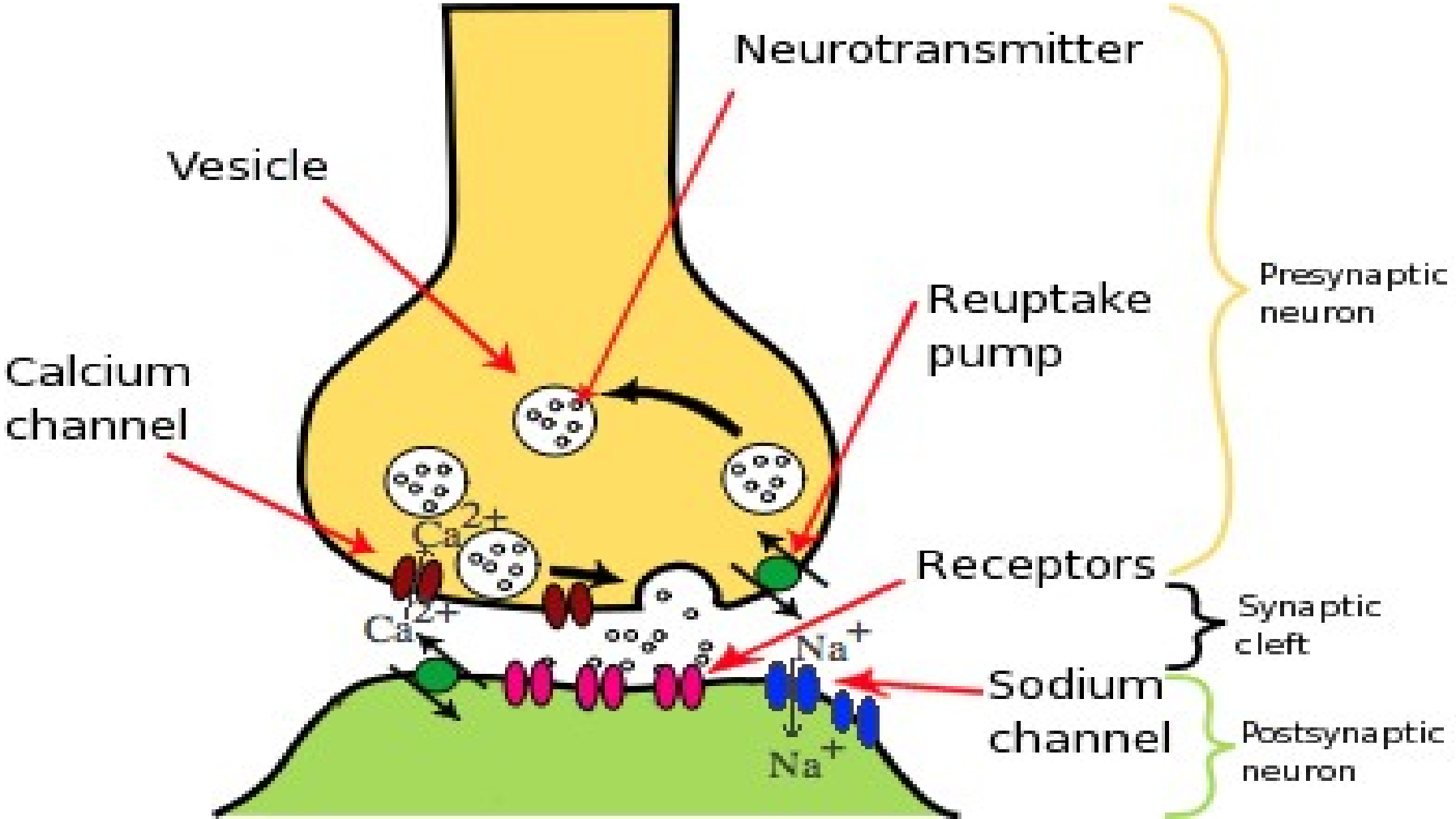
# Functions of Ionic Calcium

## Neuromuscular excitability



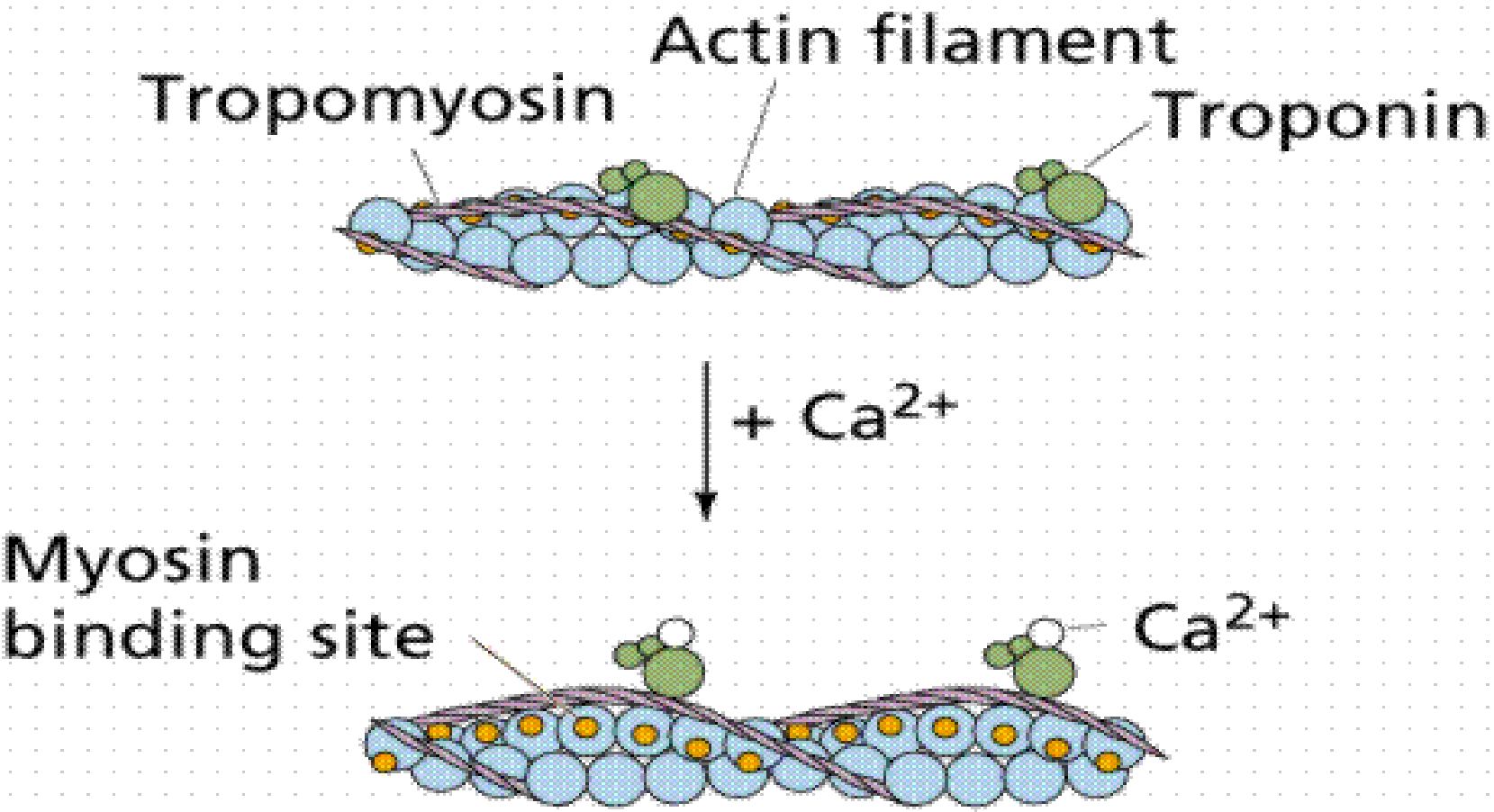
# Functions of Ionic Calcium

## Synaptic transmission



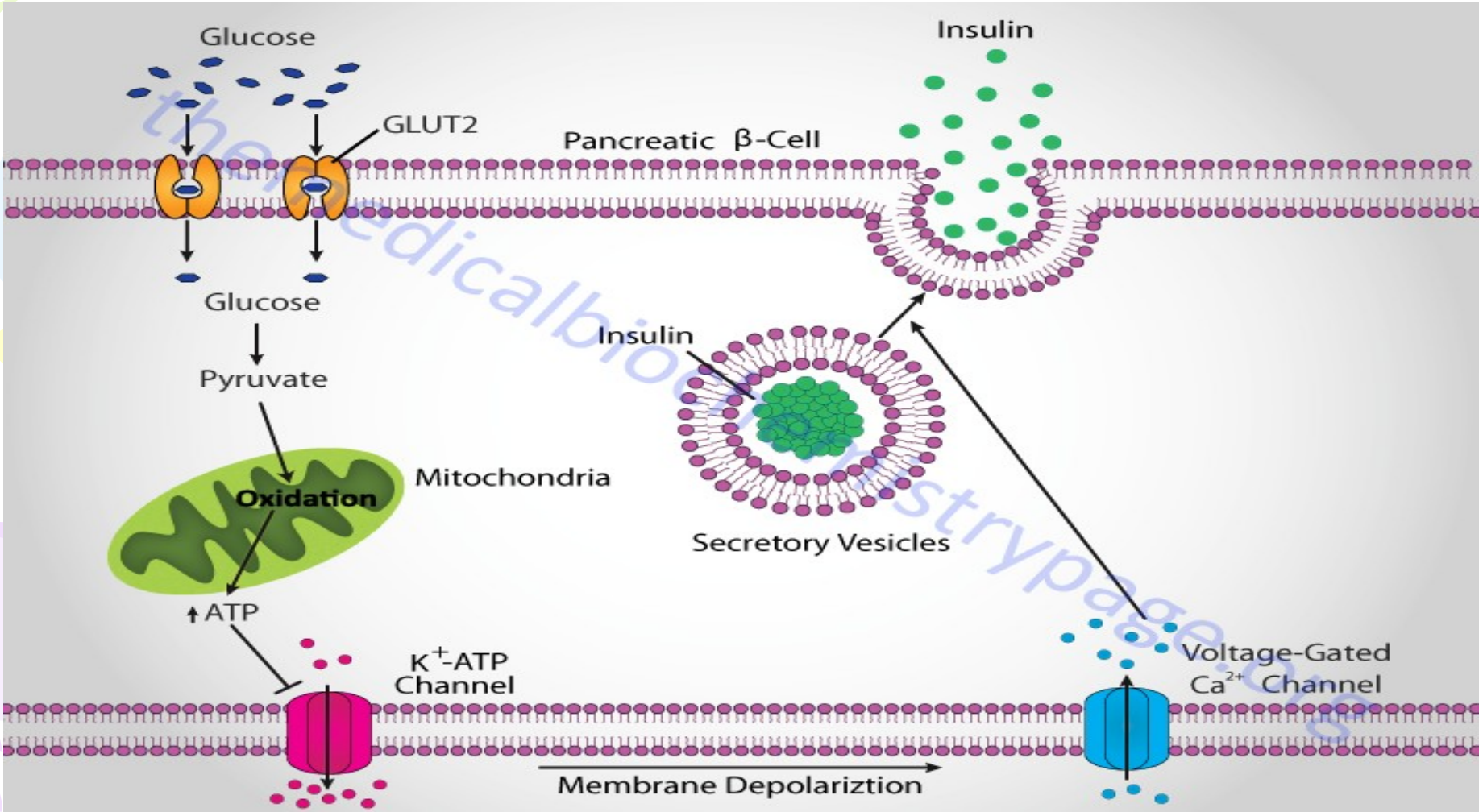
# Functions of Ionic Calcium

## Muscle



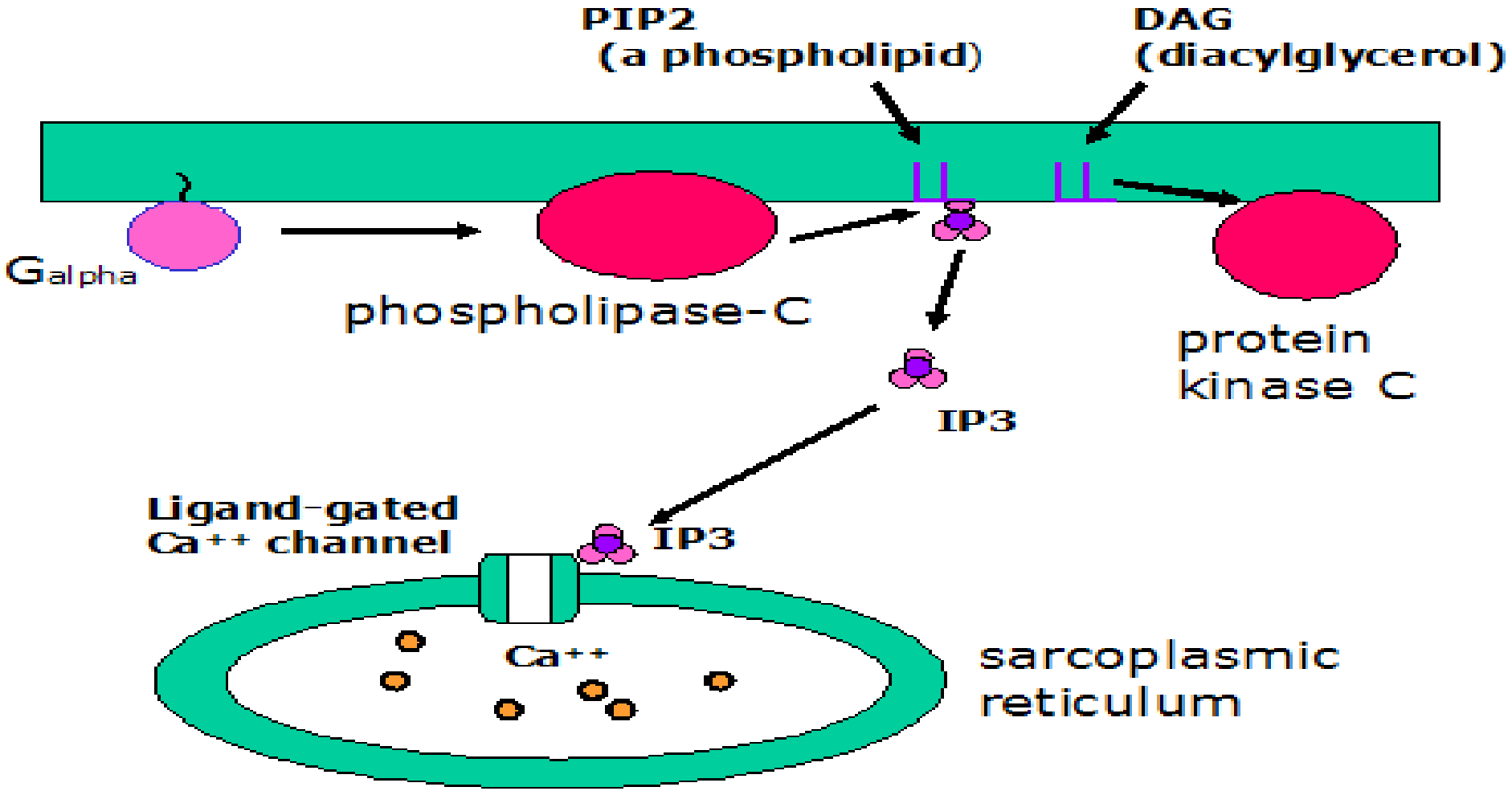
# Functions of Ionic Calcium

## Hormone secretion



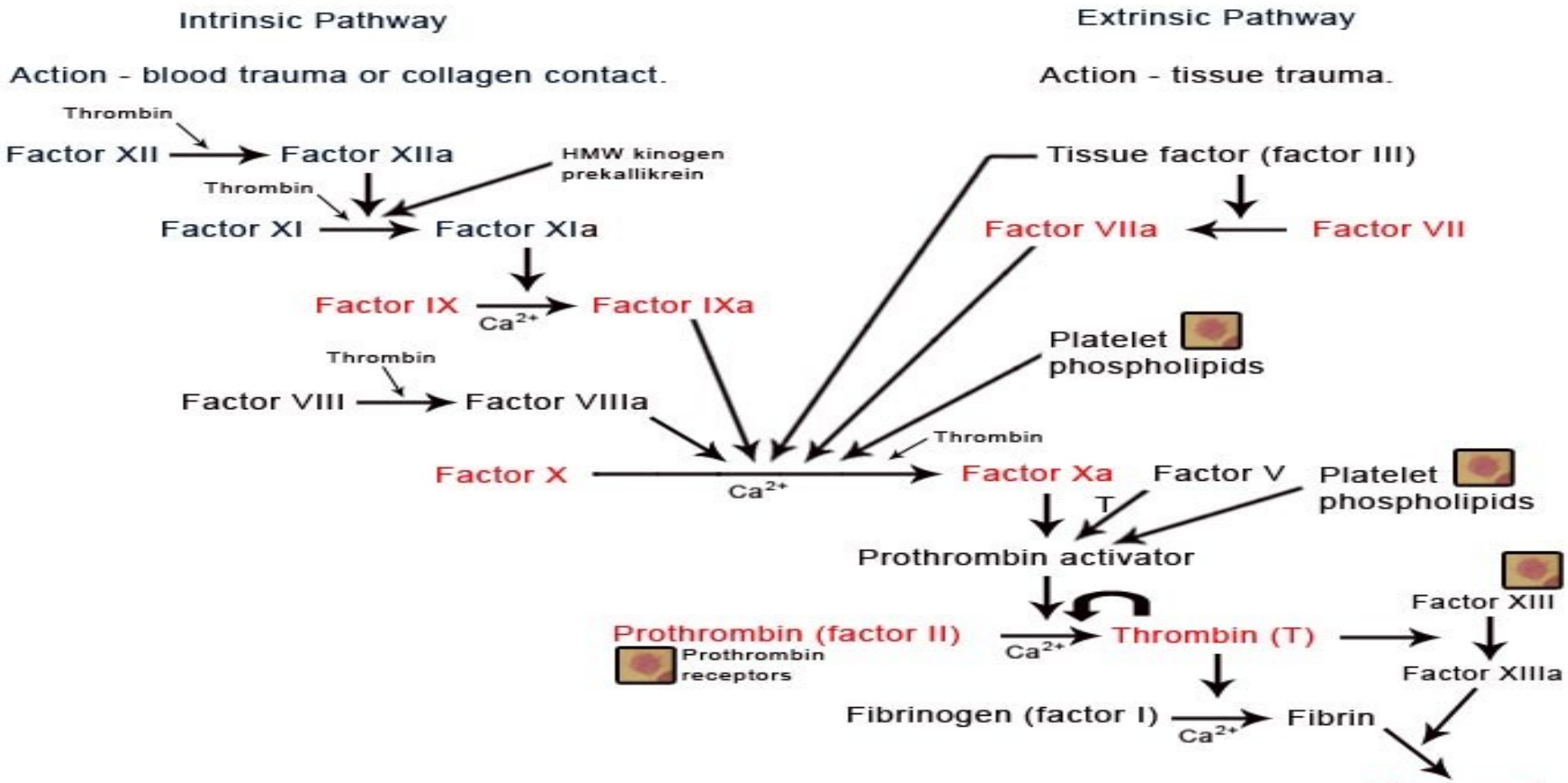
# Functions of Ionic Calcium

## Hormone action



# Functions of Ionic Calcium

## Coagulation



# Functions of Ionic Calcium

- **Calcium is necessary for:**
  - Bone and teeth formation hydroxyapatite crystals
  - Neuromuscular excitability $Ca^{++}$ stabilize voltage gated $Na^{+}$ channeles
  - Synaptic transmission caused by $Ca^{++}$ influx into presynaptic terminal
  - Muscle contraction caused by $Ca^{++}$ efflux from sarcoplasmic reticulum
  - Hormone secretion as in insulin, catecholamines, ADH and oxytocin release
  - Secondary messenger in many hormonal actions
  - Blood coagulation $Ca^{++}$ is a cofactor required at most factor activation steps
  - Activation of some enzymes
  - Cell proliferation, motility and ciliary action
  - Maintain normal permeability of cell membrane and capillaries

# Calcium homeostasis = Maintenance of plasma free $Ca^{++}$

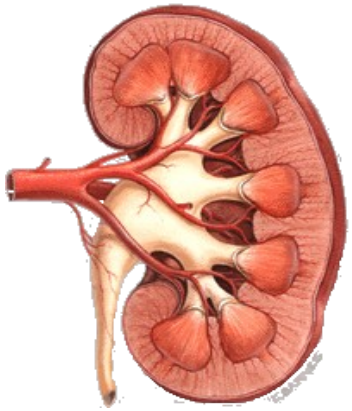
# 3 hormones involved in Calcium homeostasis

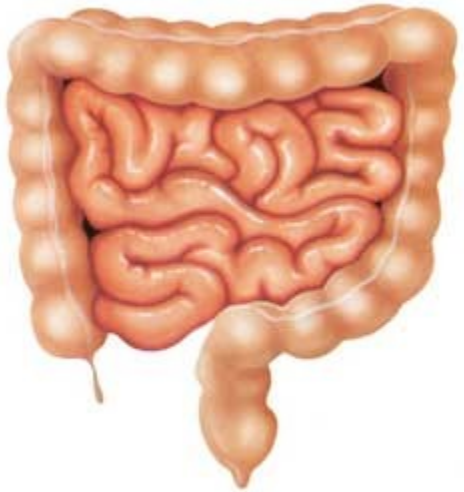
- **Parathyroid hormone (PTH)**
  Ca elevating hormone
- **Calcitriol (1,25 DHCC) Steroid H.**
  Ca elevating hormone
- **Calcitonin**
  Ca lowering hormone

- **Which control Calcium:**
  - **Absorption**
  - **Storage**
  - **Excretion**

# 3 Organs involved in Calcium Homeostasis

- Bone
- Kidney
- Gastrointestinal tract



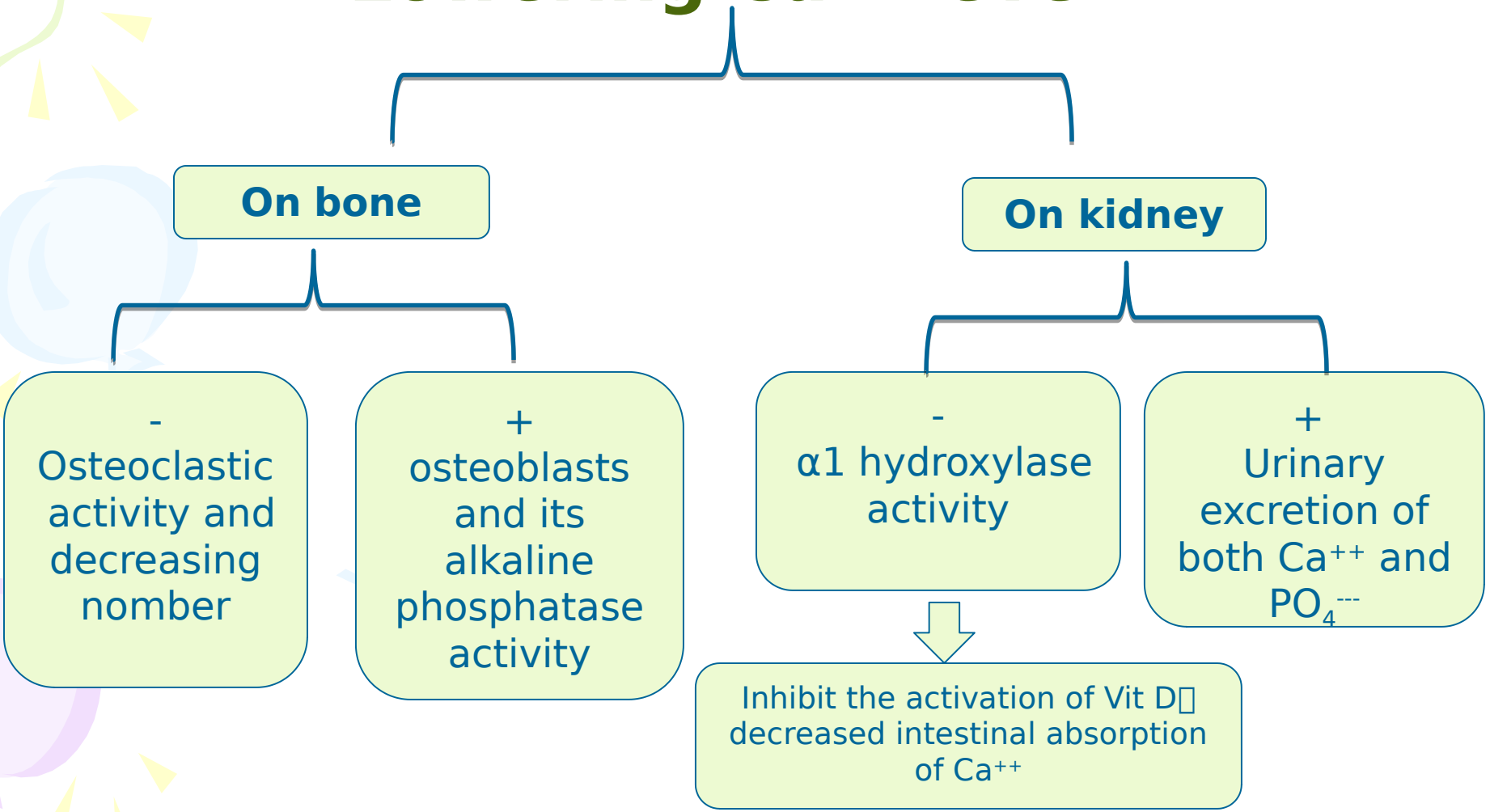


# Calcitonin= Thyrocalcitonin

- Secreted by thyroid parafollicular cells.
- Polypeptide hormone (32 aa).
- Its action is mediated by cAMP.
- Lowers $Ca^{++}$ and $PO_4^{---}$ levels by acting on bone and kidney.
- Antagonize PTH as regard $Ca^{++}$ but similar to PTH as regard $PO_4^{---}$
- An increase in serum $Ca^{++}$ level stimulate its secretion.
- Many GIT hormones e.g. Gastrin, Glucagon, CCK, Secretin. As well as Estrogen and Dopamine stimulate its release.

# Calcitonin Actions

## Lowering $Ca^{++}$ level



# $D_3$

## Obtained from:

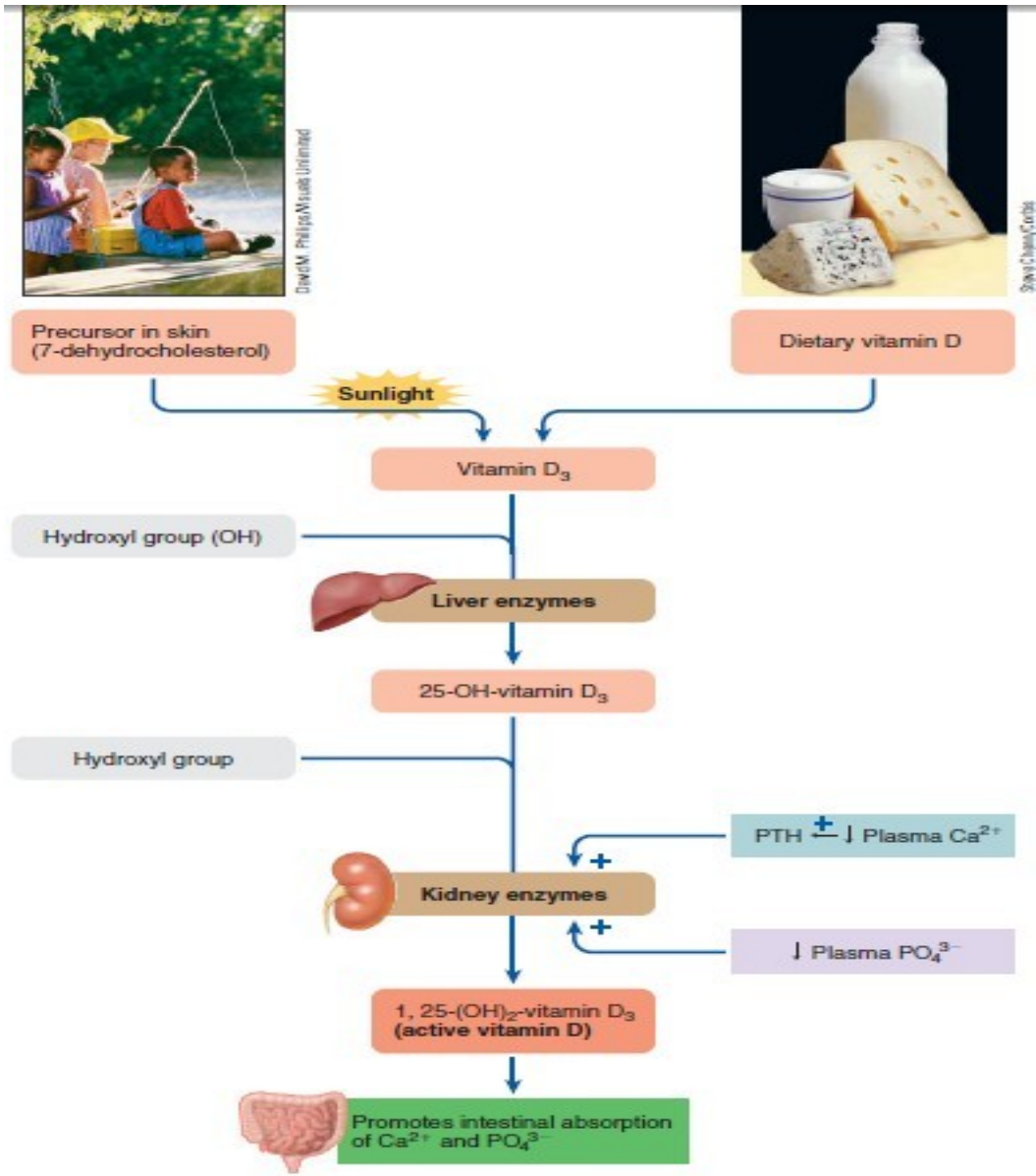
***Diet**

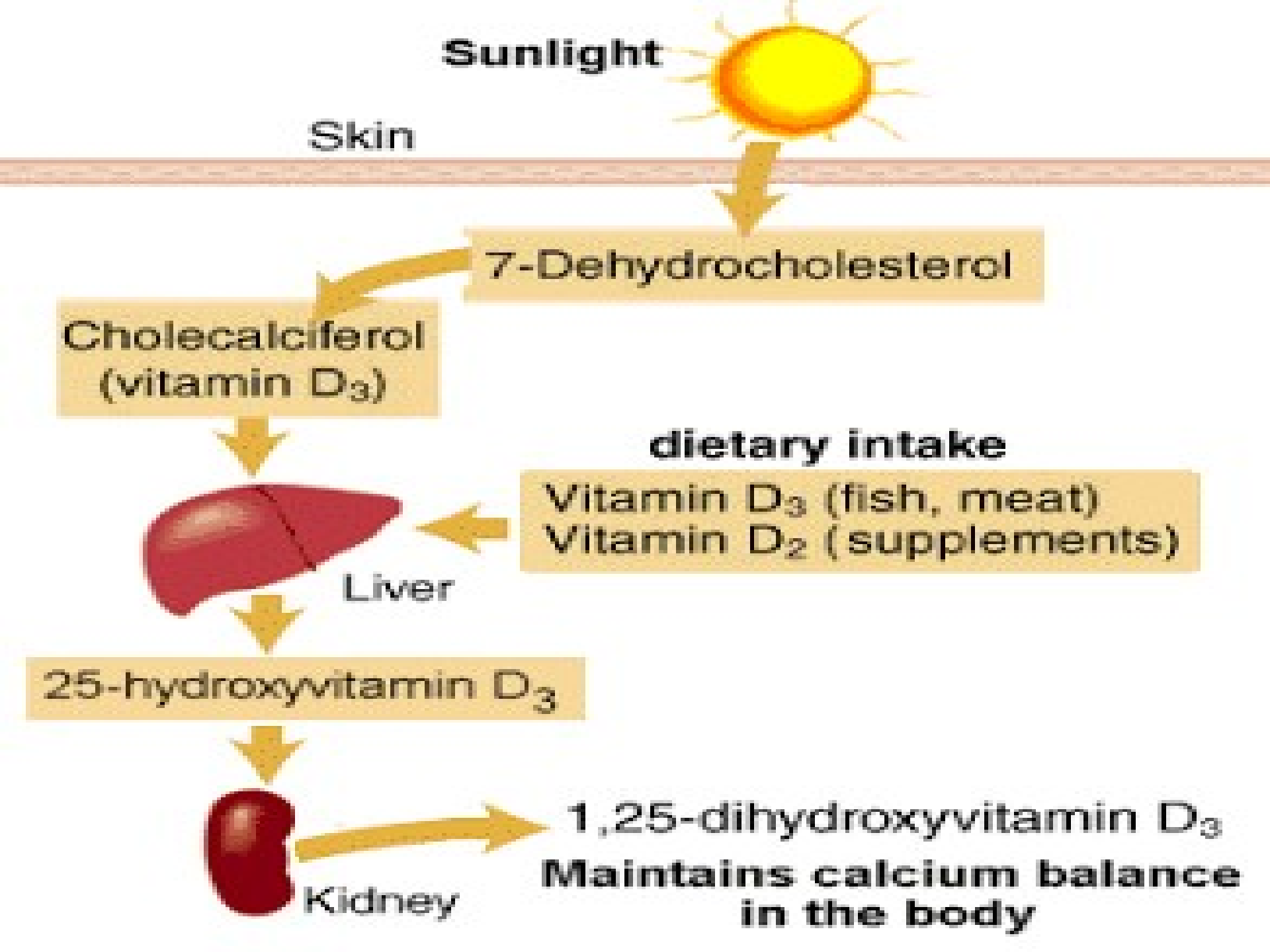
***Synthesized in the body**

- Cholecalciferol formed in the **skin** by sun ultraviolet rays.
- 25-OH Cholicalciferol formation in **liver.**
- 1,25 DHCC formation in **kidney**

  *(Controlled by PTH).*

* Plasma calcium concentration inversely regulates 1,25 DHCC




Sunlight
Skin
7-Dehydrocholesterol
Cholecalciferol
(vitamin $D_3$)
dietary intake
Vitamin $D_3$ (fish, meat)
Vitamin $D_2$ (supplements)
Liver
25-hydroxyvitamin $D_3$
Kidney
1,25-dihydroxyvitamin $D_3$
Maintains calcium balance
in the body

# Calcitriol

**Being steroid hormone; it acts on cytoplasmic receptor**

## actions

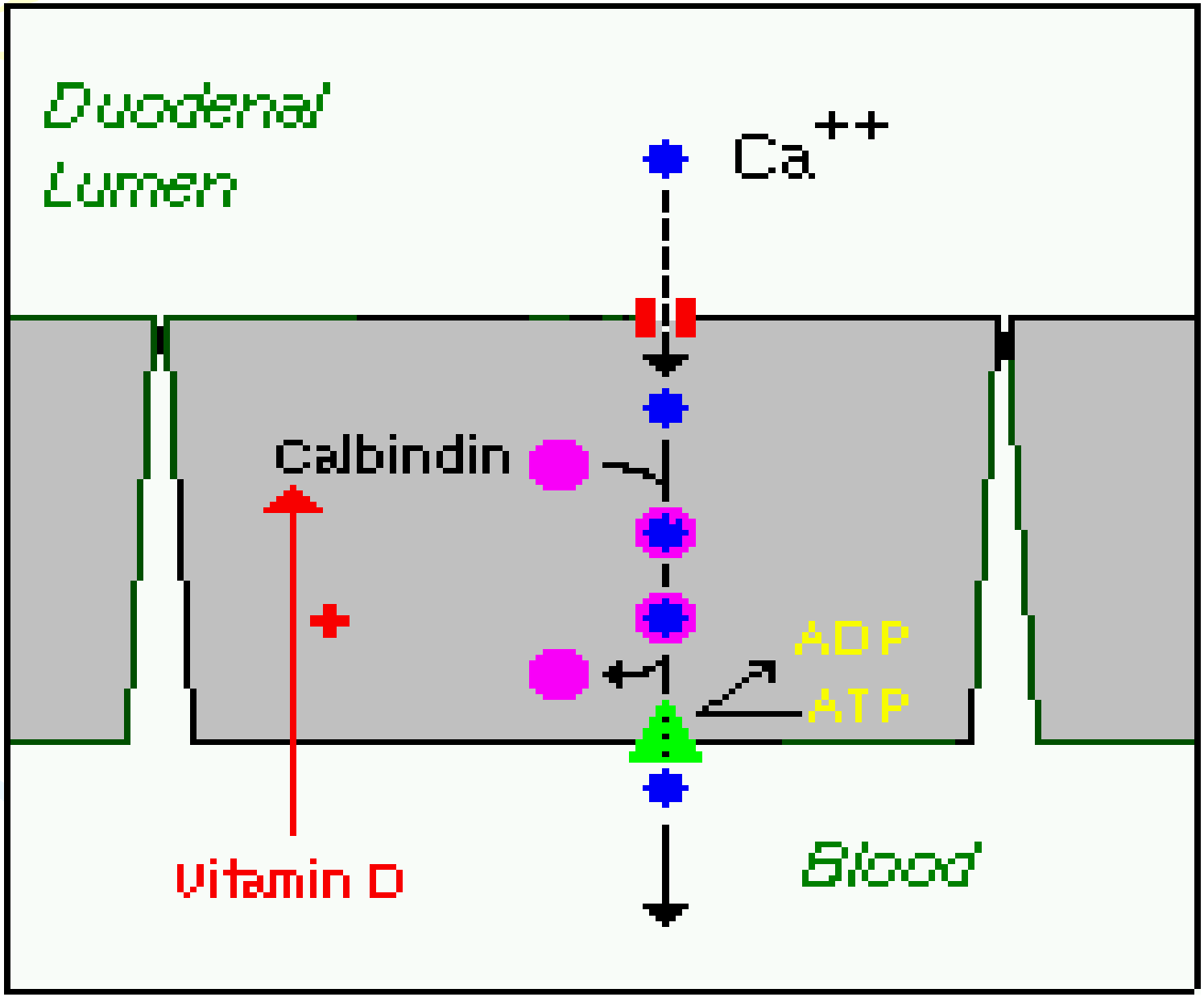
**On Intestine:**
**Main action**
Increase absorption of $Ca^{++}$ and $PO_4^{---}$ by increasing **Calbindin D& Ca ATPase pump**

**On kidney:**
+ reabsorption of both $Ca^{++}$ and $PO_4^{---}$

**On bone:**
Depends on $Ca^{++}$ and $PO_4^{---}$ concentration

**High**
+
osteoblasts

**Low**
+
osteoclasts




Calcitriol action on intestine

# Calcium Homeostasis

## Parathyroid Hormone (PTH)

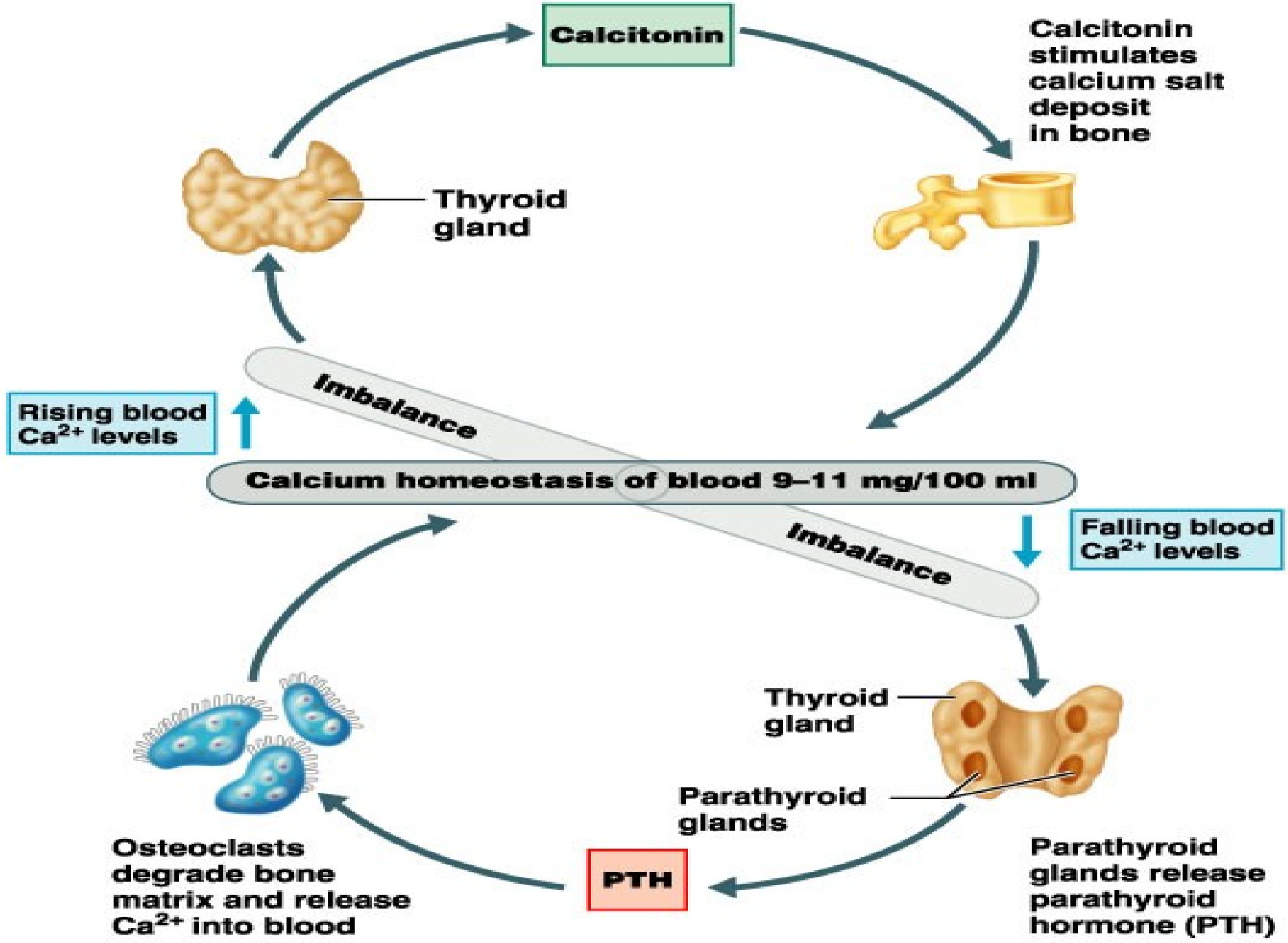
- Increases calcium ion levels by:
  1. Stimulating osteoclast
  2. Increasing intestinal absorption of calcium (indirectly)
  3. Decreasing calcium excretion at kidney

## Calcitonin (Thyrocalcitonin)

- Decreases calcium ion levels by:
  1. Inhibiting osteoclast
  2. Decreasing intestinal absorption of calcium (indirectly)
  3. Increasing calcium excretion at kidney

## Calcitriol (1,25 DHCC)

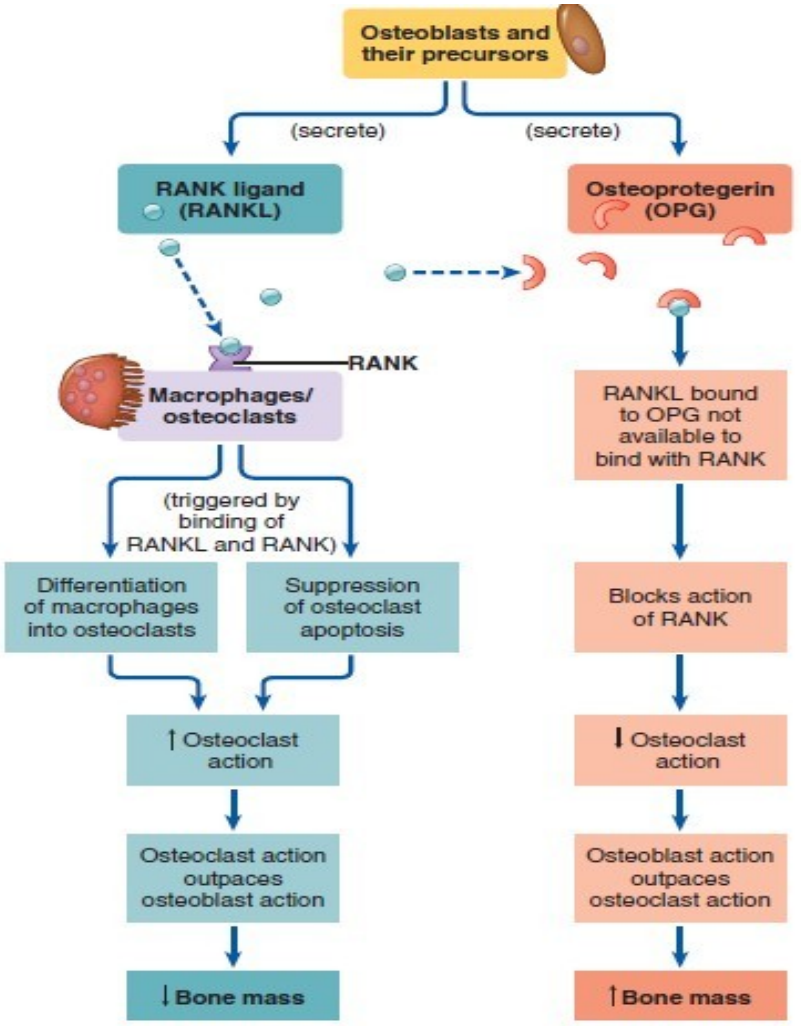
- Increases calcium ion level by:
  1- Increasing intestinal absorption
  2- Decreasing urinary excretion
  3- On bone: according to calcium level??????



# Other hormones affecting bone and $Ca^{++}$ metabolism

- **Estrogens:** slow down bone loss (+osteoblast) (↑ OPG= gene osteoprotegerin).
- **Insulin:** (↑ bone formation).
- **Growth Hormone** (↑ $Ca^{++}$absorption).
- **Insulin like Growth factors (IGFs):** as GH (↑ $Ca^{++}$ absorption).
- **Glucocorticoids:** ↓ $Ca^{++}$ level by inhibiting its gut absorption & ↑ renal excretion - ↓bone formation & inhibit osteoblast and stimulate osteoclast.

**Prolonged use of glucocorticoids produce osteoporosis (bone loss)**




Role of osteoblasts in governing osteoclast development and activity

# Lecture Quiz

**Concerning Vitamin D, all of the following true except:**

A) It can be formed in the body.

B) It increases intestinal absorption of $Ca^{++}$.

C) It is activated in the kidney by conversion to 1,25 DHCC.

D) The formation of its active form is inhibited by PTH.

E) The formation of 1,24,25 HCC or 1,24 DHCC is stimulated by Calcitonin.

# Lecture Quiz

**The serum calcium level:**

A) Is normally about 30mg%.

B) Influences the rate of PTH secretion by an action on the hypothalamus.

C) Is approximately 10% ionized & 90% combined.

D) Becomes less ionized when blood PH falls.

E) Greatly affect the neuromuscular excitability.

# SUGGESTED TEXTBOOKS

1. Ganong’s review of medical physiology

   25th edition

2. Gyuton and Hall 13th edition


THANK YOU
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